		2002/11/1 9 11:12	USPAT; US-PGPUB; EPO; JPO; DERWENT	translocation adj domain	180	L10	BRS	10
		2002/11/1 9 11:11	UB; EPO; ERWENT	light adj chain	9210	Ь9	BRS	9
		2002/11/1 9 11:11	USPAT; US-PGPUB; EPO; JPO; DERWENT	(1 or 2) same 7	0	L8	BRS	8
		2002/11/1 9 11:10	USPAT; US-PGPUE; EPO; JPO; DERWENT	(erythrina or (glycine adj max) or (arachis adj hypogaea) or (bandeirea adj simplicifolia) ) same lectin	127	Ь7	BRS	7
		2002/11/1 9 11:10	USPAT; US-PGPUE; EPO; JPO; DERWENT	(1 or 2) same 3	10	L5	BRS	٥
		2002/11/1 9 10:54	USPAT; US-PGPUE; EPO; JPO; DERWENT	(1 or 2) same 4	2	16 1	BRS	И
		2002/11/1 9 10:54	USPAT; US-PGPUE; EPO; JPO; DERWENT	lectin same (galactose or galactosyl or aceylgalactosamine) same bind\$3	401	L4	BRS	4
		2002/11/1 9 10:53	USPAT; US-PGPUE; EPO; JPO; DERWENT	lectin	11914	L3	BRS	ω
		2002/11/1 9 10:53	USPAT; US-PGPUE; EPO; JPO; DERWENT	botulinum adj (toxin or neurotoxin)	492	L2	BRS	Ν
		2002/11/1 9 10:52	USPAT; US-PGPUE; EPO; JPO; DEFWENT	clostridial adj neurotoxin	83	L1	BRS	<u> </u>
Err or Def ini tio	Com men ts	Time Stamp	DB 3	Search Text	Hits	۲ #	Туре	

0			2002/11/1 9 11:15	~•	6 same 13		L14 0	BRS	14
0			2002/11/1 9 11:15	USPAT; US-PGPUB; EPO; JPO; DERWENT	39709 control\$4 same 7 (transmission or pain)	39709	L13	BRS	13
0			2002/11/1 9 11:13	USPAT; US-PGPUE; EPO; 2002 JPO; DERWENT 9 11	6 same 3	N	Ь12	BRS	12
0			2002/11/1 9 11:12	USPAT; US-PGPUE; EPO; 2002 JPO; DERWENT 9 11	9 same 10 same (1 or 2)	6	L11	BRS	11
10 10 11	Err or Def ini tio	Com men	Time Stamp	DB 3	Search Text	Туре L # Hits	۲ #	Туре	

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT

11:18:01 ON 19 NOV 2002

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- L2 19773 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
- L3 20134 S L1 OR L2
- L4 145857 S LECTIN
- L5 9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR

ACETYLGALACTOSAMINE) (P)

- L6 1 S L3 (P) L5
- L7 48 S L3 (P) L4
- L8 26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
- L9 15675 S L4 (P) (GALACTOSE OR GALACTOSYL OR

ACETYLGALACTOSAMINE)

- L10 1 S L9 (P) L3
- L11 6 S L8 (P) (CONJUGATE OR COVALENT?)
- L12 5 S L11 NOT L6
- L13 88211 S LIGHT CHAIN
- L14 433 S TRANSLOCATION DOMAIN
- L15 4 S L3 (P) L13 (P) L14
- L16 0 S L15 (P) L4

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                                                                SESSION
FULL ESTIMATED COST
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FILE 'CAPLUS' ENTERED AT 11:18:01 ON 19 NOV 2002
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FILE 'SCISEARCH' ENTERED AT 11:18:01 ON 19 NOV 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)
FILE 'AGRICOLA' ENTERED AT 11:18:01 ON 19 NOV 2002
=> s clostridial neurotoxin
           881 CLOSTRIDIAL NEUROTOXIN
1.1
=> s (botulinum toxin) or (botulinum neurotoxin)
         19773 (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
=> s l1 or l2
L3
         20134 L1 OR L2
=> s lectin
        145857 LECTIN
=> s 14 (p) (galactose or galactosyl or acetylgalactosamine) (p) bind?
          9696 L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
               BIND?
=> s 13 (p) 15
                                                  1 .
             1 L3 (P) L5
=> d 16 1 ibib abs
     ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                         1999:249106 CAPLUS
DOCUMENT NUMBER:
                         130:276767
TITLE:
                                         ***galactose*** - ***binding***
                         Conjugates of
                           ***lectins*** and ***clostridial***
                           ***neurotoxins*** as analgesics
INVENTOR(S):
                         Duggan, Michael John; Chaddock, John Andrew
PATENT ASSIGNEE(S):
                         The Speywood Laboratory Limited, UK; Microbiological
                         Research Authority
SOURCE:
                         PCT Int. Appl., 50 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
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PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9917806 Al 19990415 WO 1998-GB3001 19981007

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,

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          RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
              FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
              CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                             19990415
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      AU 9893574
                        A1
                             19990427
                                             AU 1998-93574
                                                              19981007
      AU 741456
                        B2
                             20011129
      ZA 9809138
                        Α
                             19990527
                                             ZA 1998-9138
                                                              19981007
      EP 996468
                        A1
                             20000503
                                             EP 1998-946571
                                                              19981007
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
      JP 2001518522
                        T2
                             20011016
                                             JP 2000-514674
                                                              19981007
PRIORITY APPLN. INFO.:
                                          GB 1997-21189
                                                         A 19971008
                                          WO 1998-GB3001 W 19981007
AB
     A class of novel agents that are able to modify nociceptive afferent
      function is provided. The agents may inhibit the release of
     neurotransmitters from discrete populations of neurons and thereby reduce
     or preferably prevent the transmission of afferent pain signals from
     peripheral to central pain fibers. They comprise a ***galactose***
        ***binding***
                          ***lectin***
                                          linked to a deriv. of a
        ***clostridial***
                              ***neurotoxin*** . The deriv. of the
        ***clostridial***
                              ***neurotoxin***
                                                 comprises the L-chain, or a
      fragment thereof, which includes the active proteolytic enzyme domain of
     the light (L) chain, linked to a mol. or domain with membrane-
     translocating activity. The agents may be used in or as pharmaceuticals
     for the treatment of pain, particularly chronic pain.
REFERENCE COUNT:
                          6
                                THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d his
      (FILE 'HOME' ENTERED AT 11:17:28 ON 19 NOV 2002)
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L2
          19773 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
L3
          20134 S L1 OR L2
L4
         145857 S LECTIN
L5
           9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
              1 S L3 (P) L5
L6
-> p 10 (p) 14
L7
            48 L3 (P) L4
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PROCESSING COMPLETED FOR L7
             26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
=> S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
         15675 L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
=> s 19 (p) 13
L10
             1 L9 (P) L3
=> s 18 (p) (conjugate or covalent?)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L75 (P) '
T.1.1
             6 L8 (P) (CONJUGATE OR COVALENT?)
<u>=> s ll1 not l6</u>
L12
             5 L11 NOT L6
=> d 112 1-5 ibib abs
L12 ANSWER 1 OF 5
                       MEDLINE
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ACCESSION NUMBER:

DOCUMENT NUMBER:

2002470902

22218001

MEDLINE

PubMed ID: 12105193

Inhibition release of neurotransmitters from rat dorsal root gangli by a novel \*\*\*conjugate\*\*\* TITLE:

Clostridium \*\*\*botulinum\*\*\* \*\*\*toxin\*\*\* endopeptidase fragment and Erythrina cristagalli

\*\*\*lectin\*\*\*

**AUTHOR:** Duggan Michael J; Quinn Conrad P; Chaddock John A; Purkiss John R; Alexander Frances C G; Doward Sarah; Fooks Sarah J;

Friis Lorna M; Hall Yper H J; Kirby Elizabeth R; Leeds Nicola; Moulsdale Hilary J; Dickenson Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Shone Clifford C; Foster

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down,

Salisbury, Wiltshire SP4 OJG, United Kingdom.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Sep 20) 277 (38)

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY:

DOCUMENT TYPE:

United States Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020917

> Last Updated on STN: 20021026 Entered Medline: 20021024

AΒ \*\*\*Clostridial\*\*\* \*\*\*neurotoxins\*\*\* potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LH(N)/A) of the type A neurotoxin from Clostridium botulinum has been coupled to a \*\*\*lectin\*\*\* obtained from Erythrina cristagalli to form a novel \*\*\*conjugate\*\*\* \*\*\*conjugate\*\*\* exhibits an in vitro selectivity for nociceptive This afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical \*\*\*conjugates\*\*\* prepared between E. cristagalli \*\*\*lectin\*\*\* and either natively sourced LH(N)/A or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LH(N)/A \*\*\*conjugate\*\*\* variant. The duration

of action of inhibition of neurotransmitter released by the \*\*\*conjugate\*\*\* in vitro is assessed and is comparable with that observed with Clostridium \*\*\*botulinum\*\*\* \*\*\*neurotoxin\*\*\* Finally, in vivo electrophysiology shows that these in vitro actions have biological relevance in that sensory transmission from nociceptive afferents through the spinar cord is significantly attenuated. These data demonstrate that the potent endopeptidase activity of \*\*\*clostridial\*\*\*

\*\*\*neurotoxins\*\*\* can be selectively retargeted to cells of interest and that inhibition of release of neurotransmitters from a neuronal population of therapeutic relevance to the treatment of pain can be achieved.

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:228744 CAPLUS

DOCUMENT NUMBER: 134:247267

INVENTOR(S):

TITLE: Clostridial neurotoxin targeted conjugates for

inhibition of secretion from non-neuronal cells Foster, Keith Alan; Chaddock, John Andrew; Purkiss,

John Robert; Quinn, Conrad Padraig

PATENT ASSIGNEE(S): Microbiological Research Authority, UK

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE -----WO 2001021213 A2 20010329 WO 2000-GB3669 20000925

WO 2001021213 A3 20020711 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

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ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                      A2 20020904
                                          EP 2000-962721
                                                          20000925
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.:
                                        GB 1999-22554
                                                         A 19990923
                                        WO 2000-GB3669
                                                        W 20000925
AΒ
     A method of treatment of disease by inhibition of cellular secretory
     processes is provided. The method has particular application in the
     treatment of diseases dependent on the exocytotic activity of endocrine
     cells, exocrine cells, inflammatory cells, cells of the immune system,
     cells of the cardiovascular system, and bone cells. Agents and compns.
     therefor, as well as methods for manufg. these agents and compns., are
     provided. In a preferred embodiment a clostridial neurotoxin,
     substantially devoid of holotoxin binding affinity for neuronal cells of
     the presynaptic muscular junction, is assocd. with a targeting moiety.
     The targeting moiety is selected such that the clostridial toxin conjugate
     so formed may be directed to a non-neuronal target cell to which the
     conjugate may bind. Following binding, a neurotoxin component of the
     conjugate, which is capable of inhibition of cellular secretion, passes
     into the cytosol of the target cell by cellular internalization
     mechanisms. Thereafter, inhibition of secretion from the target cell is
     effected.
L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                         2000:706999 CAPLUS
DOCUMENT NUMBER:
                         133:261538
TITLE:
                         Use of a lectin or lectin conjugate for modulation of
                         C-fiber activity, and therapeutic use thereof
INVENTOR(S):
                         Foster, Keith Alan; Chaddock, John Andrew; Quinn,
                         Conrad Padraiq
PATENT ASSIGNEE(S):
                         Microbiological Research Authority, UK
SOURCE:
                         PCT Int. Appl., 62 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                   KIND DATE
                                         APPLICATION NO. DATE
                     ----
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     WO 2000057897 A1 20001005
                                         WO 2000-GB1247 20000331
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
            CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
            ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
            LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
            {\tt ZW}, {\tt AM}, {\tt AZ}, {\tt BY}, {\tt KG}, {\tt KZ}, {\tt MD}, {\tt RU}, {\tt TJ}, {\tt TM}
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1165114
                                        EP 2000-914295
                      A1 20020102
                                                           20000331
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:
                                       GB 1999-7429
                                                        A 19990331
                                                       W 20000331
                                       WO 2000-GB1247
AΒ
     The invention relates to the treatment of pain and to compds. that
     modulate C-fiber activity. In particular, the invention relates to the
               ***lectin*** in the manuf. of a medicament for modulation of
     C-fiber neuron activity, and to
                                     The ***lectin***
                         <u>***conjugates*** comprise a ***lectin***</u>
     coupled to a peptide or protein, wherein the peptide or protein is
     substantially free of ***Clostridial***
                                                  ***neurotoxin***
                                                                     enzvme
     activity. The invention also concerns methods for manufg. the
```

\*\*\*conjugates\*\*\* . The compds. and compns. described have particular application in the treatment of diseases of which C-fiber activity is a component. Such diseases include pain, inflammation, psoriasis and other

C-fiber related conditions.

LU, LV, MA, MD, MG MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SR

SL, TJ, TM, TR, TT, TZ, UA, UG,

t, VN, YU,

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2000:144760 CAPLUS

DOCUMENT NUMBER:

132:175838

TITLE:

Compounds inhibiting exocytosis in mucus-secreting cells or neurotransmitter release from neurons that control or direct mucus secretion for treatment of

mucus hypersecretion

INVENTOR (S):

Quinn, Conrad Padraig; Foster, Keith Alan; Chaddock,

John Andrew

PATENT ASSIGNEE(S):

Microbiological Research Authority, UK

SOURCE:

PCT Int. Appl., 30 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010598	A2	20000302	WO 1999-GB2806	19990825
WO 2000010598	ΔZ	20000615		

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2341429 AA20000302 CA 1999-2341429 19990825 AU 9955250 A1 20000314 AU 1999-55250 19990825 EP 1107794 A2 20010620 EP 1999-941754 19990825

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002523377 T2 20020730 JP 2000-565918 19990825 PRIORITY APPLN. INFO.: GB 1998-18548 A 19980825 WO 1999-GB2806 W 19990825

AB A method of treating mucus hypersecretion, the causative factor in chronic obstructive pulmonary disease (COPD), asthma, and other clin. conditions involving COPD, comprises administering a compd. that inhibits exocytosis in mucus secreting cells or neurons that control or direct mucus secretion. Also described is a compd., for use in the treatment of hypersecretion of mucus, which inhibits mucus secretion by inhibiting mucus secretion by mucus secreting cells, and/or inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: DOCUMENT NUMBER:

2002:520037 BIOSIS PREV200200520037

TITLE:

Characterisation of a novel \*\*\*conjugate\*\*\* 

AUTHOR (S):

fragment and E. cristagalli \*\*\*lectin\*\*\* Ling, R. J. (1); Fretwell, R.; Alexander, F.; Fooks, S.; Leeds, N.; Jameson, K.; Hall, Y.; Kirby, E.; Chaddock, J.;

Shone, C.

CORPORATE SOURCE:

(1) Centre for Applied Microbiology and Research, Porton

Down, Salisbury, Wiltshire, SP4 0JG UK

SOURCE:

Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R28. print. Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins

Hannover, Germany June 08-12, 2002

ISSN: 0028-1298.

DOCUMENT TYPE: LANGUAGE:

Conference English

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(FILE 'HOME' ENTERED AT 11:17:28 ON 19 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 11:18:01 ON 19 NOV 2002

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          20134 S L1 OR L2
 L4
          145857 S LECTIN
            9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
 L5
 L6
               1 S L3 (P) L5
L7
              48 S L3 (P) L4
              26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
L8
           15675 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
L9
L10
              1 S L9 (P) L3
               6 S L8 (P) (CONJUGATE OR COVALENT?)
L11
L12
               5 S L11 NOT L6
=> s light chain
         88211 LIGHT CHAIN
=> s translocation domain
L14
           433 TRANSLOCATION DOMAIN
=> s 13 (p) 113 (p) 114
             4 L3 (P) L13 (P) L14
=> s l15 (p) l4
L16
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          19773 S (BOTULINUM TOXIN) OR (BOTULINUM NEUROTOXIN)
L3
          20134 S L1 OR L2
L4
         145857 S LECTIN
L5
           9696 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE) (P)
L6
              1 S L3 (P) L5
L7
             48 S L3 (P) L4
L8
             26 DUPLICATE REMOVE L7 (22 DUPLICATES REMOVED)
L9
          15675 S L4 (P) (GALACTOSE OR GALACTOSYL OR ACETYLGALACTOSAMINE)
L10
              1 S L9 (P) L3
L11
              6 S L8 (P) (CONJUGATE OR COVALENT?)
L12
              5 S L11 NOT L6
L13
          88211 S LIGHT CHAIN
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L15
             4 S L3 (P) L13 (P) L14
L16
              0 S L15 (P) L4
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